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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/004,494	11/02/2001	Yung-Fu Chang	1258-006 CIP	9399

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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/004,494	CHANG, YUNG-FU	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-11 and 26-50* is/are pending in the application.

4a) Of the above claim(s) *32-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-11,26-31 and 47-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11/2/2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application filed November 2, 2001is a continuation in part of 09/358,322, filed July 21, 1999, now abandoned.

Applicant's amendment filed July 23, 2005, has been received and entered. The specification has been amended. Claims 3, 4, 12-25, 51-65 have been canceled. Claims 1, 2, 5-11, 26-50 are pending.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1, 2, 6-11, 26-31 and 47-50, in the reply filed on November 3, 2004, was acknowledged.

Applicant maintains that the restriction requirement be withdrawn and request that the finality be withdrawn. See page 11, section 3 of Applicant's amendment. Applicants comments have been noted, however no new arguments have been provided in traverse of the restriction requirement, nor any specific reason for removing the finality of the requirement. Additionally, it is noted that claims of some of the non-elected inventions have been canceled. The restriction requirement is maintained for the reasons of record.

The requirement is still deemed proper and is maintained as FINAL.

Claims 1, 2, 5-11, 26-50 are pending. Claims 32-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election)

requirement in the reply filed on November 3, 2004. Claims 1, 2, 5-11, 26-31, 47-50, drawn to DNA and DNA vaccines and methods of making

Specification

The disclosure objected to because the third page of claims is incorrectly numbered is withdrawn.

The amendment to the specification has obviated the basis of the objection. See also Applicant's amendment, page 11, section 4.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 10 and 11 stand objected to under 37 CFR 1.75 as being a substantial duplicate of claim 6.

Applicants summarize the embodiments of the claims and note that claims 10 and 11 recite embodiments that are not in the prior claim 6. See Applicants' amendment, pages 12-13, section 5. Applicants' arguments have been fully considered, but not found persuasive.

As indicated previously, the recitation in claims 10 and 11 are noted, however neither change the scope of the product in claim 6 as they simply set forth an intended use of the claimed product. The simple recitation of how the product is going to be used, fails to differentiate the product of claims 10 and 11 from claim 6 or from each other. Though claim 10 implies and intended use in a method of delivery and claim 11 indicates a particular host to which it is used, they both cover the same thing as they are drawn to the claimed product set forth in claim 6, or even each other, i.e. comparing claims 10 and 11 with themselves. Applicants' do not point to any difference in the functional or physical scope of the claims, only that dependent claims recite embodiments that are not found in claim 6. This argument is not found persuasive because the scope of the claims as they are drawn to the product are found to be the same.

It is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP 706.03(k).

Claim Rejections - 35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-11, 26-31 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Initially, it is noted that claims 1, 2 and 47-50 are withdrawn from the rejection because they have other potential enabled uses that would be recognized in the art. Examiner agrees with arguments by Applicant, that a product requires only one enabled use. With respect to the methods of claims 47-50, as with the product these only require that a recombinant DNA be made, and at most that the protein that is potentially expressed is immunogenic. Since most protein sequences are immunogenic in some context, the rejection is withdrawn over these claims.

However, with the remaining claims 5-11, 26-31, each of these specifically recite and encompass a "vaccine" which is differentiated from any general sequence because it must meet a functional limitation of providing a protective immunity, and in this case to *E. canis*. Applicant notes the requirements of 35 USC 112, first paragraph, and case law that supports that complex experimentation is not necessarily "undue" (see pages 13-16), and that the present specification provides a working example (page 16) with respect to consideration of the Wands factors. Examiner acknowledges the requirements of 35 USC 112, first paragraph, and the cited case law in support of Applicant's arguments, however maintains that providing a DNA vaccine as encompassed by the claims would require undue experimentation. The working example is noted, and that the discussion suggests that some specific protein epitope may provide a level of protection considered to be prophylactic rising to the level for use as a vaccine, however the working example is with administration of a protein, not a recombinant DNA to be expressed. Again, the physiological art in general is acknowledged to be unpredictable (MPEP 2164.03), and as set forth in the prior office action there are several art recognized limitations and unpredictability issues regarding the delivery of a polynucleotide as demonstrated in gene

delivery protocols, that include: vector to be used for gene expression, production of effective concentration of the candidate protein, delivery of the protein or gene to target cell, sustained expression and production of the candidate protein *in vivo*, and maintaining an effective level of the protein *in vivo*. In making an argument of enablement Examiner has cited the general review of the art by Verma *et al.* and art relevant to making DNA vaccines by Bohm *et al.*

Applicant has pointed the Written Description guidelines, and have argued that Examiner's basis of rejection is in contrast to the requirement of enablement instantly made, in that once an antigen is known, an antibody to said antigen is described (pages 16-17). It is noted that the instant rejection is not written description, but enablement, and more specifically enablement of the prophylactic affect encompassed by claiming a vaccine. Examiner does not disagree with USPTO Written Description guidelines, and as much as it concerns the basis of the instant rejection of enablement has argued that antibodies to *E. canis* were known as evidenced by the serum of infected dogs , however it has been argued that this general antigenicity alone is insufficient to satisfy the enablement requirements of a vaccine. Again as noted previously, the specification and the art of record teach that no successful vaccine for *E. canis* has been developed to date (instant specification page 4, first paragraph), even though dogs will develop an immune response to the whole bacteria of *E. canis*.

Examiner agrees that an invention does not have to be demonstrated by reduction to practice, however it is maintained that it has to be enabled for the breadth of the claims, in this case as it is drawn to using any fragment of the cloned genomic sequence to produce a DNA vaccine to *E. canis*. Examiner notes that the specification provides guidance for the construction of recombinant vectors and recites means of delivery of a polynucleotide to a subject which are

known in the art, however the specification is silent with respect to guidance or examples for the use of the assigned open reading frames as immunogenic fragments in a vaccine for *E. canis*. Again, three points of enablement are at issue; first, the specification demonstrates that antisera from dogs can react with a protein which is encoded by the genomic fragment, however it is unclear what protein epitope or open reading frame encodes the protein which reacts with the antisera. More specifically, it is unclear that any of the five proposed reading frames produce a protein which is normally encoded by *E. canis*. Further, it is unclear that production of a protein from one of the five deduced open reading frames encode a protein from *E. canis* which would produce an immune response in a dog. Second, the proposed open reading frames in the proper context can encode a protein and there are examples in the art that demonstrate that one can produce an immune response when one injects enough of almost any protein. However, the specification does not demonstrate that any of the proposed reading frames encode an immunogenic epitope, and further, it is not clear that the proteins encoded by the proposed open reading frames produces a prophylactic immune response to *E. canis* infection encompassed by the full scope of the claim. Finally, the claimed vaccine is a DNA vaccine, and the specification relies in great part on delivery methods and expression systems taught by others for the ability to infect the host cells and for the production of the proper amount of the foreign protein to induce an immune response, however there is no guidance nor demonstration that these methods and systems can be used for expression of the proposed open reading frames which result in a prophylactic immune response.

Examiner agrees that enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention, but "Whether undue

experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). In the instant case, the specification is not enabling for the claimed invention because the art of gene delivery, in particular the delivery of a DNA vaccine which encode undefined immunogenic epitopes, is highly unpredictable as recognized in the prior art and because the specification as filed does not provide sufficient guidance, evidence and exemplification as to how an artisan would have carried out the claimed methods for expression of any of the specific cloned genes from *E. canis*, wherein the encoded protein stimulates the appropriate immune response such that a prophylactic effect is achieved in said subject. It is maintained that it would require extensive research to understand the fundamental biology of the system for the development of a vaccine to *E. canis* from the proposed gemonic fragment. Applicants have described deduced open reading frames of a cloned genomic fragment of *E. canis* which may encode protein epitopes, but essentially all of the work required to ultimately define and develop these genomic sequences into methods to produce a prophylactic immune response has been left for others.

Claims 9 and 29 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant agues that the vectors claimed are commercially available and argue that meeting the deposit requirement is not necessary (three exhibits are provided to support their assertion). See section 6(a), page 19 of Applicant's amendment.

With respect to the vectors pcDNA3 and pC1, Examiner agrees that they are commercially available and that the complete sequence is known in the art that a skilled artisan could make the plasmid if ever the vector were not available. However, with respect to VR1012 and VR1020, Examiner acknowledges the teaching of Wizel *et al.* however this fails to demonstrate the public availability of the vectors. A search of Vical's products fails to provide support for Applicants assertion that the vectors are publicly available, or sufficient teachings that one could reproduce the vectors (see information provided from Vical's product listing). Since the invention consists of specific vectors for expression of the DNA and the methods require the use of the vectors, and the vectors are recited and essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the cell lines are not so obtainable or available, the requirements of 35 U.S.C. 112, regarding "how to make", may be satisfied by a deposit of vectors.

Again, it is noted that review of the specification does not provide any specific sequence information for any of the four claimed vectors. If a deposit has been made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific cell lines have been deposited under the Budapest Treaty and that the cell lines will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement.

It the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, Applicant may provide assurance

of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that

(a) during the pendency of this application, access to the invention will afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request of for the effective life of the patent, whichever is longer; and,

(d) a test of viability of the biological material at the time of deposit (see 37 CFR 1.807); and,

(e) the deposit will be replaced if it should ever become inviable.

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required one of skill in the art undue experimentation to practice the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 47, 48, 49, 50 stand rejected under 35 U.S.C. 102(b) as being anticipate by Lewis *et al.* (1994).

Applicant summarizes the embodiments of the claims (page 20) and argues that the cited reference fails to anticipate the claimed composition (pages 20-21). Applicant argues that Lewis *et al.* fail to teach a "recombinant DNA" and that the sequence elicits an immune response to *E. canis*. See section 6(b), pages 19-21 of Applicant's amendment. Applicant's arguments have been fully considered, but not found persuasive.

Initially, it is noted that Applicant does not argue the sequence of Lewis *et al.* does not share homology with the claimed sequences, only that it is not recombinant and that it will not induce an immune response, in particular to *E. canis*. The instant rejection has been made and maintained in light of the breadth of the claims in light of the guidance of the instant specification. With respect to the term recombinant, this is broad general term recognized in the art, and the cloning of the sequences out of the genome and their characterization as disclosed by Lewis *et al.* would constitute a recombinant sequence since it is out of the endogenous content. Further, it is noted that the sequence is manipulated as a DNA molecule. With respect to the ability of the sequence to elicit an immune response, Examiner would agree that Lewis *et al.* fails to teach the use of the sequence as a vaccine or its ability to elicit a response to *E. canis*, however in evaluating the breadth of the claims in light of the teachings of the specification, Examiner is left to interpret the claims structurally to encompass any homologous sequence to that disclosed and claimed. The instant specification does not point to any specific sequence be necessary nor required for eliciting an immune response, nor do Applicant's arguments differentiate the breadth of the claimed sequences from that of Lewis *et al.* The claims broadly encompass any polynucleotide sequence which encodes an amino acid sequence that can elicit an immune response and vectors capable of expressing said protein. As suggested by Applicant, the

rejection relies in part on inherency of the sequence, and given that sequences share structural similarity as demonstrated by their homology, and given the guidance of the instant specification, it is maintained that the sequence specifically disclosed shares stretches of homology that would encode some portion of a protein set forth in SEQ ID NO: 3, 5, 7 and 11. Lewis *et al.* teach the use of expression vectors to screen for inserts, therefore the proteins encoded by the sequences inserted in the vectors of the isolated clones serve a sequence capable of producing a protein that could serve and are capable of producing an immune response.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

As noted previously, the complete sequence of each of the SEQ ID NOs appear to be free of the prior art of record because the prior art of record fails to teach or suggest the complete polynucleotide sequences or a method of creating a vaccine with said sequences. However, the breadth of the claims encompass any portion or immunogenic fragment of these sequences.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

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